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Laser-Induced Luminescence Studies and Crystal Structure of the Europium(III) Complex of 1,4,7,10-Tetrakis(carbamoylmethyl)-1,4,7,10-tetraazacyclododecane. The Link between Phosphate Diester Binding and Catalysis by Lanthanide(III) Macrocyclic Complexes

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Solution and solid-state properties of the Eu(III) complex of the tetraamide macrocyclic ligand TCMC (TCMC = 1,4,7,10-tetrakis(carbamoylmethyl)-1,4,7,10-tetraazacyclododecane) are investigated as part of an effort to develop lanthanide(III) macrocyclic catalysts. $[Eu(TCMC)(H_2O)](CF_3SO_3)_3 \cdot 2CH_3OH$ crystallizes in the centrosymmetric monoclinic space group $P2_1/n$ with $a = 12.0571(15)$ Å, $b = 13.2196(20)$ Å, $c = 25.4250(40)$ Å; $\beta = 91.673(11)°$, $V = 4050.8$ Å^3, and $Z = 4$. The structure was solved and refined to $R = 4.02\%$ and $R_w = 4.33\%$ for 3510 reflections with $F > 6\sigma(F)$. ($R = 7.04\%$, $R_w = 6.48\%$ for all 5322 independent reflections.) Four stereoisomers (two enantiomeric pairs) of the $[Eu(TCMC)(H_2O)]^{3+}$ cation appear in the crystal. The structure is disordered, containing two overlapping diastereomers that are interrelated by different conformations of the 1,4,7,10-tetraazacyclododecane ring defining the asymmetric unit. Two enantiomers are related to these by operations of the second kind (i, n-glide). The nine-coordinate Eu(III) center has a 4:4:1 coordination geometry formed by the octadentate TCMC ligand and a single bound water molecule. The laser-induced luminescence excitation band of a single crystal of $[Eu(TCMC)(H_2O)](CF_3SO_3)_3 \cdot 2CH_3OH$ resolves into two peaks, suggesting that each diastereomer gives rise to a separate excitation peak. Similarly, the luminescence excitation spectrum of a solution of $[Eu(TCMC)]^{3+}$ in water indicates that two species are present in solution. Luminescence lifetime measurements in H_2O and in D_2O indicate that the europium(III) ion in the TCMC complex has 1.5 ± 0.5 bound water molecules. The ^{31}P NMR resonance of diethyl phosphate is monitored at 18 ± 2 °C, pH 7.4, upon addition of $[Eu(TCMC)]^{3+}$ as well as upon addition of several lanthanide(III) complexes that are catalysts for RNA cleavage. No binding of diethyl phosphate to $[Eu(TCMC)]^{3+}$ is observed. The hexadentate Schiff-base complex $[La(L^1)]^{3+}$ binds to diethyl phosphate with a binding constant of 47.7 ± 0.5 M^{-1}.

Introduction

The catalytic properties of aqueous solutions of lanthanide(III) ions have attracted much interest. Lanthanide ions promote rapid RNA cleavage,[1−4] hydrolysis of phosphoric anhydrides[5,6] and phosphate esters.[7−10] Cleavage of DNA[11] and phosphate esters[12] is promoted by lanthanide ions in the presence of oxygen or peroxide. Ce(IV) ions promote rapid hydrolysis of phosphate diesters and DNA cleavage.[13,14] In addition, there is much interest in the catalytic properties of lanthanide ion complexes. Macrocyclic complexes that are kinetically inert to lanthanide ion release may find use as artificial ribonucleases for the sequence-specific cleavage of RNA.[15,16]

We have prepared lanthanide(III) macrocyclic complexes and evaluated their catalytic properties.[17−19] Several complexes have been shown to promote or to catalyze cleavage of RNA.[20−22] These include lanthanide(III) complexes of tetraazamacrocycles as well as lanthanide(III) complexes of hexadentate Schiff-base macrocycles (Chart 1). For the complexes of the tetraazamacrocycles, catalytic activity depends markedly on the lanthanide ion. $[Eu(TCMC)]^{3+}$ is inactive in promoting RNA cleavage under conditions where the analogous lanthanum(III) complex promotes substantial cleavage of the RNA oligomers A_{12}−A_{18}.[22]

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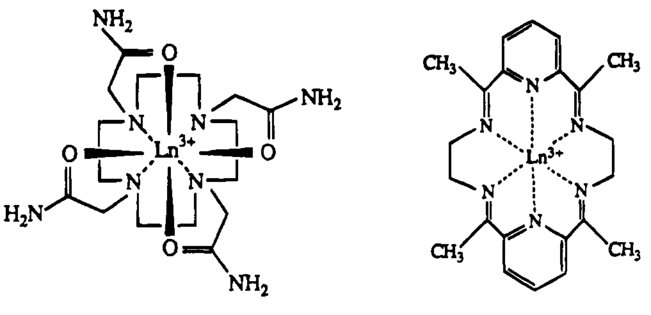
Chart 1. Lanthanide(III) Macrocyclic Complexes



$[Ln(TCMC)]^{3+}$ Ln = La, Eu

$[Ln(L^1)]^{3+}$ Ln = La, Eu

Similarly, the lanthanum(III) complex of THP (1,4,7,10-tetrakis-(2-hydroxypropyl)-1,4,7,10-tetraazacyclododecane) is more active in promoting RNA cleavage than is the analogous Eu(III) complex.[21] These dramatic differences in reactivity are attributed in part to the smaller number of coordination sites of the Eu(III) complexes compared to the La(III) complexes. In support of this hypothesis, the solid state structure of the $[La(TCMC)(EtOH)(CF_3SO_3)]^{2+}$ cation has ten coordination sites for the La^{3+} ion with two sites occupied by solvent or a counterion. ^1H and ^{13}C NMR studies of the $[La(TCMC)](CF_3SO_3)_3$ complex indicate that the structure in solution is similar to that in the solid state. The values for the free energy of activation for rotation about the C$-$N bond of the amide groups and the ^{13}C NMR chemical shifts of the amide carbonyl groups are different for the complex and for the free ligand, suggesting that the amide groups coordinate to the lanthanum(III) ion in solution. On the basis of comparisons to analogous complexes such as $[Eu(DOTA)]^-$, it was anticipated that the $[Eu(TCMC)]^{3+}$ cation would have only one coordination site for binding small molecules. The crystal structure of $[Eu(TCMC)(H_2O)](CF_3SO_3)_3{\cdot}2CH_3OH$ is described here.

In order to better understand the basis for the catalytic behavior of lanthanide(III) complexes and in particular to rationalize the inactivity of $[Eu(TCMC)]^{3+}$ as a catalyst, we have investigated some of the aqueous solution properties of lanthanide(III) complexes. It is of interest to determine whether the number of available coordination sites in solution for binding small molecules such as water is similar to that observed in the solid state structure of the complex. Laser-induced luminescence excitation spectroscopy of Eu(III) is a powerful method for the characterization of europium(III) complexes and is used here to study the Eu(III) complex of TCMC. In addition, phosphate diester binding to several lanthanide(III) complexes is studied by use of ^{31}P NMR. Binding properties of $[Eu(TCMC)]^{3+}$ are compared to those of other lanthanide(III) complexes that promote RNA cleavage.

Experimental Section

An Orion Research 510 digital ion analyzer equipped with a temperature compensation probe was used for all pH measurements. All ^{31}P NMR spectra were recorded by use of a Varian 400 XL spectrometer. NMR sample temperatures are measured by use of a thermocouple located near the probe.

The lanthanide(III) complexes $[Eu(L^1)](Cl)(CH_3CO_2)_2$, $[La(L^1)](NO_3)_3$,[23] $[Ln(TCMC)](CF_3SO_3)_3$ (Ln = La, Eu)[22] were prepared as described previously. Crystals of $[Eu(TCMC)(H_2O)](CF_3SO_3)_3$ suitable for a single-crystal X-ray diffraction study were obtained by dissolution of the complex in a minium amount of absolute methanol followed by the addition of methylene chloride (70% yield). $P(O)(OH)(OEt)_2$ was purchased from Kodak and was used as received.

Luminescence Studies. Excitation spectra and lifetime measurements were carried out using a Quantel series YG581C pulsed (10 Hz) Nd:YAG pumped tunable dye laser (Model TDL50, 70 mJ/pulse). Additional details of this system have been described previously.[24] The $^7F_0 \rightarrow {}^5D_0$ transition of the Eu^{3+} ion (577$-$581 nm) was excited by using a mixture of Rhodamine 590 (Exciton) and Rhodamine 610 (Kodak) dyes. The $^5D_0 \rightarrow {}^2F_2$ state was monitored at 614 nm. Deconvolution of the component peaks of an excitation spectrum was accomplished using the program Spectrum.[25] Data were also analyzed by use of the program Peakfit (Jandel Scientific). Each of the programs employs algorithms based on the nonlinear regression method developed by Marquardt.[26] Minimization of χ^2 and plots of the weighted residuals of a fit of the data were used to judge the quality of the fit.

Experiments were typically carried out with 0.01 mM solutions of Eu(III) complex in the pH range 6.33$-$8.60. A 1:1 mixture of 0.01 M HEPES (*N*-(2-hydroxyethyl)piperazine-*N*′-ethanesulfonic acid) and MES (2-(*N*-morpholino)ethanesulfonic acid) buffers were used. NaCl (0.10 M) was used to maintain ionic strength. All excitation spectra ($^7F_0 \rightarrow {}^5D_0$) were recorded over the 577$-$581 nm range and resolved into excitation bands using nonlinear regression methods.

Phosphate Ester Binding Studies. Binding studies were carried out at 18 ± 2 °C at pH 7.4. Solutions typically contained tetramethylammonium chloride ($\mu = 0.1$ M) to maintain a constant ionic strength, 5$-$10 mM trimethyl phosphate as an internal reference and 2.5$-$10 mM diethyl phosphate. Solutions were prepared in a mixture of 30% D_2O and 70% H_2O. Lanthanide(III) complex concentrations ranged from 0.100 to 40 mM.

Phosphate diester binding was studied for the lanthanide(III) complexes by monitoring changes in the ^{31}P resonance of diethyl phosphate upon addition of lanthanide complex and fitting the data to the equations below. Only one ^{31}P resonance was observed for diethyl phosphate under all conditions with excess phosphate diester or with excess lanthanide(III) complex, indicating rapid exchange rates for the lanthanide(III) complexes on the NMR time scale. The observed chemical shift (δ_{obs}) is then an average of those for free and bound phosphate ester and is expressed[27] as

$$\delta_{obs} = \delta_C(f_b) + \delta_P(f_p) \qquad (1)$$

In eq 1 δ_C is the ^{31}P chemical shift of bound phosphate ester, δ_P is the ^{31}P chemical shift of free phosphate ester, f_b is the fraction of bound phosphate ester, and f_p is the fraction of free phosphate ester. With the chemical shift differences given as $\Delta = \delta_P - \delta_{obs}$ and $\Delta_{max} = \delta_P - \delta_C$, eq 2 describes the binding isotherm for a lanthanide(III) complex with a phosphate ester. [Ln] is the concentration of lanthanide complex.

$$\Delta = (\Delta_{max}K[Ln])/(1 + K[Ln]) \qquad (2)$$

Data for $[La(L^1)]^{3+}$ binding to diethyl phosphate were fit to eq 2 by a nonlinear curve-fitting routine. Standard deviations for chemical shift measurements were less than 1.5%.

Collection of Diffraction Data for $[Eu(TCMC)(H_2O)](CF_3SO_3)_3{\cdot}2CH_3OH$. A colorless crystal of maximum dimension 0.3 mm was mounted on a Siemens P2$_1$/P3 diffractometer. Data collection (Mo Kα) was carried out as described previously;[28] details are given in Table 1. A total of 5910 reflections were collected and were merged to a set of 5322 independent reflections ($R_{int} = 1.41\%$). All data were corrected for Lorentz and polarization factors and for absorption. The observed diffraction symmetry (2/m) and the systematic absences $h0l$ for $h + l = 2n+1$ and $0k0$ for $k = 2n + 1$ uniquely define the centrosymmetric monoclinic space group $P2_1/n$ (No. 14).

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Table 1. Experimental Details of the X-ray Diffraction Study of $[Eu(TCMC)(H_2O)^{3+}][CF_3SO_3^-]_3 \cdot 2CH_3OH$

Crystal Data	
empirical formula	$C_{21}H_{42}EuF_9N_8O_{16}S_3$
crystal system	monoclinic
space group	$P2_1/n$
unit cell dimensions	$a = 12.0571(15)$ Å $b = 13.2196(20)$ Å $c = 25.4250(40)$ Å $\beta = 91.673(11)°$
volume	4050.8(10) Å^3
Z	4
formula weight	1081.7
density (calc)	1.774 Mg/m^3
absorption coefficient	1.808 mm^{-1}
$F(000)$	2176
Data Collection	
diffractometer used	Siemens P2$_1$/P3
radiation	Mo Kα ($\lambda = 0.710\ 73$ Å)
temperature	298 K
monochromator	highly oriented graphite crystal
2θ range	5.0–45.0°
scan type	ω
scan speed	constant; 2.00°/min in ω
scan range (ω)	0.55°
background measurement	stationary crystal and stationary counter at beginning and end of scan, each of 25.0% of total scan time
standard reflections	3 measured every 97 reflections
index ranges	$0 \le h \le 13, 0 \le k \le 14, -27 \le l \le 27$
reflections collected	5910
independent reflections	5322 ($R_{int} = 1.41\%$)
observed reflections	5322 ($F > 0.3\sigma(F)$)
observed reflections	3510 ($F > 6.0\sigma(F)$)
absorption correction	semiempirical
min/max transmission	0.4241/0.5635
Solution and Refinement	
system used	Siemens SHELXTEL PLUS (VMS)
solution	direct methods
refinement method	full-matrix least-squares
quantity minimized	$\sum w(F_o - F_c)^2$
hydrogen atoms	riding model, fixed isotropic U
weighting scheme	$w^{-1} = \sigma^2(F) + 0.0017F^2$
number of parameters refined	516
final R indices (6σ data)	$R = 4.02\%, R_w = 4.33\%$
R indices (all data)	$R = 7.04\%, R_w = 6.48\%$
goodness-of-fit	1.00
largest and mean Δ/σ	0.001, 0.000
data-to-parameter ratio	10.3:1
largest difference peak	1.24 e Å^{-3}
largest difference hole	−0.97 e Å^{-3}

Solution of the Crystal Structure for $[Eu(TCMC)(H_2O)](CF_3SO_3)_3 \cdot 2CH_3OH$. All computations were carried out by use of the SHELXTL PLUS program package.[29] Corrections for anomalous dispersion were made to the analytical scattering factors.[30] The structure was solved by direct methods. We encountered substantial problems with refinement; these problems were eliminated when we realized that the 12-membered macrocyclic ring was "disordered". In other words, there were two diastereomers of the $[Eu(TCMC)(H_2O)]^{3+}$ ion occupying each site. Hydrogen atoms were included in calculated positions based upon d(C−H) = 0.96 Å.[31] Refinement converged with $R = 4.02\%$, $R_w = 4.33\%$ for 3510 reflections with $F > 6\sigma(F)$ and $R = 7.04\%$, $R_w = 6.48\%$ for all 5322 independent reflections. Maximum features on a final difference-Fourier synthesis ranged from −0.97 to +1.24 e$^-$/Å^3. Final atomic coordinates are listed in Table 2.

Table 2. Final Atomic Coordinates ×10^4 and Equivalent Isotropic Displacement Coefficients (Å^2 × 10^3) for $[Eu(TCMC)(H_2O)^{3+}][CF_3SO_3^-]_3 \cdot 2CH_3OH$

	x	y	z	U(eq)[a]
Eu(1)	1425(1)	2393(1)	718(1)	25(1)
O(1)	−575(5)	2182(4)	584(2)	41(2)
O(14)	859(5)	3318(4)	−54(2)	35(2)
O(16)	1024(5)	938(4)	184(2)	35(2)
O(18)	723(5)	1349(4)	1407(2)	38(2)
O(20)	492(4)	3682(4)	1181(2)	31(2)
N(1)	2732(6)	3920(6)	460(3)	50(3)
N(4)	2991(7)	1853(8)	73(3)	69(4)
N(7)	2839(7)	1072(6)	1148(4)	69(4)
N(10)	2525(6)	3155(7)	1550(3)	49(3)
N(14)	801(6)	4682(5)	−571(3)	42(3)
N(16)	1093(7)	155(6)	−590(3)	48(3)
N(18)	589(7)	−158(6)	1797(3)	57(3)
N(20)	−186(6)	4027(6)	1969(3)	49(3)
C(2)	3475(13)	3541(13)	−56(7)	23(4)
C(2′)	3617(17)	3736(15)	235(9)	51(5)
C(3)	3946(12)	2453(10)	34(6)	20(3)
C(3′)	3441(17)	3032(17)	−158(7)	46(5)
C(5)	3578(15)	774(14)	346(7)	29(4)
C(5′)	3830(18)	1402(16)	201(8)	51(5)
C(6)	3869(14)	925(12)	944(6)	32(4)
C(6′)	3474(19)	599(16)	562(10)	53(6)
C(8)	3194(15)	1530(13)	1760(7)	28(4)
C(8′)	3641(21)	1401(18)	1427(10)	71(6)
C(9)	3471(12)	2680(11)	1739(6)	25(3)
C(9′)	3103(16)	2045(17)	1818(7)	40(5)
C(11)	2915(12)	4305(10)	1347(6)	15(3)
C(11′)	3332(18)	3760(16)	1458(8)	55(5)
C(12)	3534(13)	4249(11)	827(6)	25(3)
C(12′)	2991(17)	4487(14)	1045(8)	46(5)
C(13)	2004(7)	4693(6)	211(3)	35(3)
C(14)	1172(7)	4193(6)	−150(3)	32(3)
C(15)	2407(8)	1484(7)	−403(4)	52(4)
C(16)	1441(7)	829(6)	−257(3)	36(3)
C(17)	2205(8)	179(6)	1296(4)	48(3)
C(18)	1111(8)	502(7)	1503(3)	41(3)
C(19)	1698(7)	3411(7)	1936(3)	40(3)
C(20)	627(7)	3734(6)	1673(3)	36(3)
S(1A)	−3302(2)	3685(2)	1066(1)	49(1)
O(1A)	−3757(7)	4507(7)	765(3)	92(4)
O(2A)	−2127(5)	3536(5)	1003(3)	65(3)
O(3A)	−3945(6)	2775(5)	1060(3)	65(3)
C(1A)	−3356(8)	4112(8)	1737(4)	54(4)
F(1A)	−2938(7)	3403(7)	2071(3)	109(4)
F(2A)	−4370(6)	4333(6)	1875(3)	104(3)
F(3A)	−2751(6)	4911(6)	1820(3)	104(3)
S(1B)	−337(2)	3533(2)	3388(1)	51(1)
O(1B)	527(7)	3919(6)	3087(3)	78(3)
O(2B)	−210(7)	3706(6)	3939(3)	79(3)
O(3B)	−1408(8)	3727(9)	3159(4)	126(5)
C(1B)	−213(20)	2178(12)	3311(7)	112(8)
F(1B)	714(15)	1876(9)	3520(6)	228(9)
F(2B)	−980(16)	1727(9)	3564(5)	224(9)
F(3B)	−289(10)	1898(7)	2840(4)	152(6)
S(1C)	−990(2)	3145(2)	−1673(1)	61(1)
O(1C)	−919(7)	3519(8)	−1167(3)	102(4)
O(2C)	−1405(9)	3941(7)	−2033(4)	108(4)
O(3C)	−1488(7)	2219(6)	−1802(4)	89(4)
C(1C)	441(10)	2974(10)	−1848(6)	76(5)
F(1C)	875(9)	2216(8)	−1626(8)	226(10)
F(2C)	523(9)	2813(14)	−2324(4)	218(8)
F(3C)	1060(7)	3715(7)	−1742(4)	145(5)
O(1S)	−1863(6)	56(6)	1672(3)	71(3)
O(2S)	−1638(8)	1944(9)	−370(3)	108(4)
C(1S)	−2313(14)	1010(11)	1799(6)	120(8)
C(2S)	−2802(13)	2191(11)	−353(6)	107(7)

[a] Equivalent isotropic U defined as one-third of the trace of the orthogonalized $\mathbf{U}_{ij}$ tensor.

Results

The $[Eu(TCMC)](CF_3SO_3)_3$ complex is prepared under non-aqueous conditions with methanol as a solvent.[22] This complex

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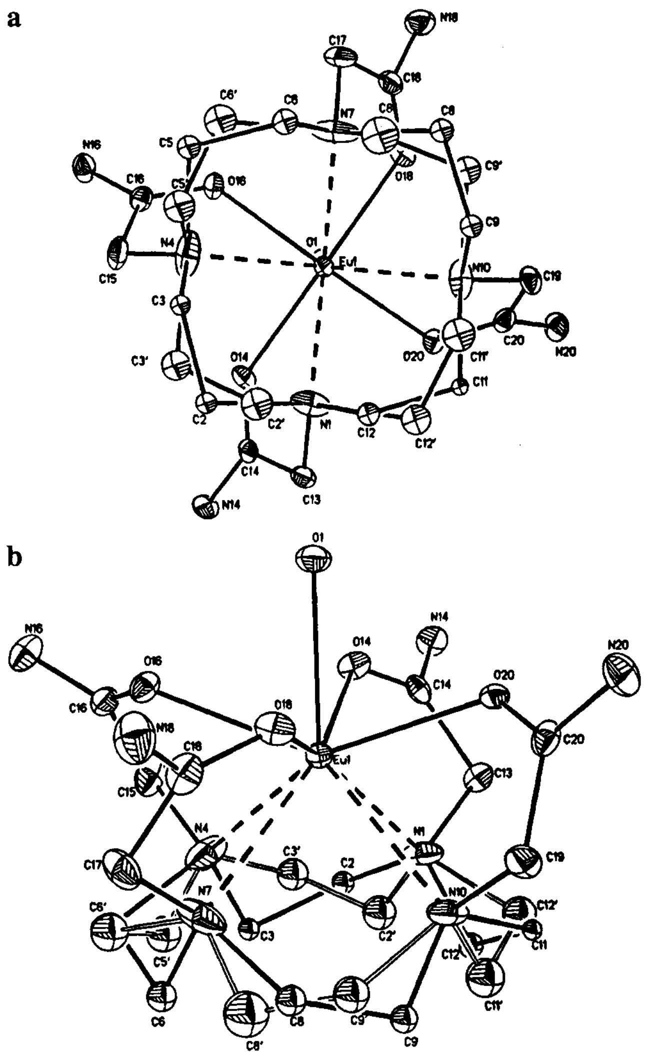

Figure 1. Labeling of atoms in the disordered $[Eu(TCMC)(H_2O)]^{3+}$ cation (ORTEP-2 diagrams; 20% vibration ellipsoids): (a) view projected onto the N_4 plane; (b) view almost perpendicular to view a, showing the different conformations of the two 12-membered rings. Atom C(5) is hidden from view by atom C(6′). One conformation of the 12-membered ring is shown with solid bonds; the other conformation is indicated by hollow bonds.

is unusual in that it is extremely kinetically inert to lanthanide ion dissociation in water at 37 °C. In the presence of Cu^{2+} as a trapping agent at pH 6.0, no dissociation (<1%) could be detected after 6 weeks at 37 °C. At higher temperatures and lower pH, dissociation of the europium(III) complex is accelerated; the half-life for dissociation is 50 days at 60 °C, pH 2.0. Thus, the europium(III) complex of TCMC is at least as inert to lanthanide ion loss as is the gadolinium(III) complex of DOTA (1,4,7,10-tetraazacyclododecane-1,4,7,10-tetraacetate).[32]

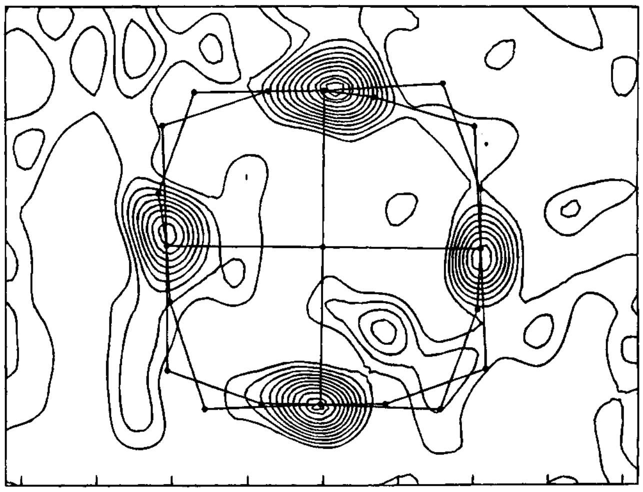

Figure 2. Electron density at the sites of the four coordinated nitrogen atoms, suggesting possible disorder at these locations also.

Table 3. Interatomic Distances (Å)

Eu(1)−O(1)	2.422(6)	Eu(1)−O(14)	2.395(5)
Eu(1)−O(16)	2.395(5)	Eu(1)−O(18)	2.404(6)
Eu(1)−O(20)	2.373(5)	Eu(1)−N(1)	2.655(7)
Eu(1)−N(4)	2.635(9)	Eu(1)−N(7)	2.653(8)
Eu(1)−N(10)	2.622(7)	O(14)−C(14)	1.243(10)
O(16)−C(16)	1.251(10)	O(18)−C(18)	1.235(11)
O(20)−C(20)	1.258(10)	N(1)−N(2)	1.686(19)
N(1)−C(2′)	1.249(23)	N(1)−C(12)	1.393(17)
N(1)−C(12′)	1.687(22)	N(1)−C(13)	1.478(11)
N(4)−C(3)	1.405(16)	N(4)−C(3′)	1.757(24)
N(4)−C(5)	1.728(21)	N(4)−C(5′)	1.211(23)
N(4)−C(15)	1.466(13)	N(7)−C(6)	1.374(18)
N(7)−C(6′)	1.806(26)	N(7)−C(8)	1.712(19)
N(7)−C(8′)	1.260(26)	N(7)−C(17)	1.463(12)
N(10)−C(9)	1.375(16)	N(10)−C(9′)	1.754(23)
N(10)−C(11)	1.676(16)	N(10)−C(11′)	1.285(23)
N(10)−C(19)	1.459(11)	N(14)−C(14)	1.318(10)
N(16)−C(16)	1.290(11)	N(18)−C(18)	1.321(12)
N(20)−C(20)	1.312(11)	C(2)−C(3)	1.561(22)
C(2′)−C(3′)	1.378(30)	C(5)−C(6)	1.562(24)
C(5′)−C(6′)	1.475(31)	C(8)−C(9)	1.558(23)
C(8′)−C(9′)	1.474(32)	C(11)−C(12)	1.540(21)
C(11′)−C(12′)	1.473(29)	C(13)−C(14)	1.494(11)
C(15)−C(16)	1.508(13)	C(17)−C(18)	1.496(13)
C(19)−C(20)	1.498(12)	S(1A)−O(1A)	1.430(9)
S(1A)−O(2A)	1.445(7)	S(1A)−O(3A)	1.431(7)
S(1A)−C(1A)	1.798(11)	C(1A)−F(1A)	1.352(13)
C(1A)−F(2A)	1.315(12)	C(1A)−F(3A)	1.298(13)
S(1B)−O(1B)	1.405(8)	S(1B)−O(2B)	1.423(7)
S(1B)−O(3B)	1.425(10)	S(1B)−C(1B)	1.808(17)
C(1B)−F(1B)	1.287(28)	C(1B)−F(2B)	1.287(26)
C(1B)−F(3B)	1.256(19)	S(1C)−O(1C)	1.380(9)
S(1C)−O(2C)	1.472(10)	S(1C)−O(3C)	1.397(8)
S(1C)−C(1C)	1.808(13)	C(1C)−F(1C)	1.256(18)
C(1C)−F(2C)	1.237(19)	C(1C)−F(3C)	1.256(16)
O(1S)−C(1S)	1.413(16)	O(2S)−C(2S)	1.443(18)

Crystal Structure of $[Eu(TCMC)(H_2O)](CF_3SO_3)_3{\cdot}2CH_3OH$. The crystallographic asymmetric unit consists of one "disordered" $[Eu(TCMC)(H_2O)]^{3+}$ cation, three triflate anions, and two methanol molecules of solvation. The composite picture of the $[Eu(TCMC)(H_2O)]^{3+}$ ion (Figure 1) clearly reveals that the 1,4,7,10-tetraazacyclododecane ring has two possible conformations. The pendent amide groups are ordered, but the ring is not. The two sites have been resolved for each macrocycle carbon atom to give essentially λ and δ conformations of each five-membered ring. However, two independent sites for the four macrocycle nitrogen atoms could not be resolved. Figure 2 shows an electron density difference map in which the four nitrogen atoms were excluded from the calculation of F_c. The contours are elongated tangentially to the ring, suggesting that the nitrogen atoms in the alternative ring images do not overlap precisely. As a result of this disorder problem, the C−C and C−N distances in the ring may have large errors associated with them. Nevertheless, it is clear that there are two diastereomers at each crystallographic site and four isomers (two enantiomeric pairs) in the crystal as a whole. Final atomic coordinates are provided in Table 2, and intramolecular distances and angles are provided in Tables 3 and 4.

The coordination environment about the europium(III) center is a (4:4:1) monocapped distorted square antiprism. The upper four coordination sites are occupied by the nitrogen atoms of

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(32) Wang, X.; Jin, T.; Comblin, V.; Lopez-Mut, A.; Merciny, E.; Desreux, J. F. *Inorg. Chem.* **1992**, *31*, 1095−1099.

Table 4. Interatomic Angles (deg)

O(1)−Eu(1)−O(14)	71.7(2)	O(1)−Eu(1)−O(16)	69.3(2)	Eu(1)−N(7)−C(6)	121.0(9)	Eu(1)−N(7)−C(6′)	99.9(8)
O(14)−Eu(1)−O(16)	84.1(2)	O(1)−Eu(1)−O(18)	70.7(2)	Eu(1)−N(7)−C(8)	106.4(7)	C(6)−N(7)−C(8)	100.8(10)
O(14)−Eu(1)−O(18)	142.4(2)	O(16)−Eu(1)−O(18)	83.3(2)	Eu(1)−N(7)−C(8′)	118.6(12)	C(6′)−N(7)−C(8′)	104.2(15)
O(1)−Eu(1)−O(20)	70.8(2)	O(14)−Eu(1)−O(20)	84.9(2)	Eu(1)−N(7)−C(17)	107.7(5)	C(6)−N(7)−C(17)	117.9(9)
O(16)−Eu(1)−O(20)	140.1(2)	O(18)−Eu(1)−O(20)	82.5(2)	C(8)−N(7)−C(17)	99.8(9)	Eu(1)−N(10)−C(9)	119.5(8)
O(1)−Eu(1)−N(1)	130.0(2)	O(14)−Eu(1)−N(1)	64.3(2)	Eu(1)−N(10)−C(9′)	100.1(7)	Eu(1)−N(10)−C(11)	103.7(6)
O(16)−Eu(1)−N(1)	125.6(2)	O(18)−Eu(1)−N(1)	147.2(2)	C(9)−N(10)−C(11)	106.5(9)	Eu(1)−N(10)−C(11′)	116.9(10)
O(20)−Eu(1)−N(1)	82.5(2)	O(1)−Eu(1)−N(4)	127.2(2)	C(9′)−N(10)−C(11′)	107.3(12)	Eu(1)−N(10)−C(19)	106.7(5)
O(14)−Eu(1)−N(4)	79.7(2)	O(16)−Eu(1)−N(4)	64.3(2)	C(9)−N(10)−C(19)	116.6(8)	C(11)−N(10)−C(19)	101.5(8)
O(18)−Eu(1)−N(4)	124.9(3)	O(20)−Eu(1)−N(4)	149.5(3)	N(1)−C(2)−C(3)	111.1(12)	N(1)−C(2′)−C(3′)	110.3(17)
N(1)−Eu(1)−N(4)	67.1(3)	O(1)−Eu(1)−N(7)	127.1(2)	N(4)−C(3)−C(2)	103.6(11)	N(4)−C(3′)−C(2′)	113.6(15)
O(14)−Eu(1)−N(7)	146.9(3)	O(16)−Eu(1)−N(7)	79.7(2)	N(4)−C(5′)−C(6′)	105.4(18)	N(7)−C(6)−C(5)	101.9(13)
O(18)−Eu(1)−N(7)	63.7(2)	O(20)−Eu(1)−N(7)	125.2(3)	N(7)−C(6′)−C(5′)	113.7(15)	N(7)−C(8)−C(9)	111.2(11)
N(1)−Eu(1)−N(7)	102.9(2)	N(4)−Eu(1)−N(7)	67.3(3)	N(7)−C(8′)−C(9′)	103.5(19)	N(10)−C(9)−C(8)	106.4(12)
O(1)−Eu(1)−N(10)	128.4(2)	O(14)−Eu(1)−N(10)	125.6(2)	N(10)−C(9′)−C(8′)	113.4(15)	N(10)−C(11)−C(12)	111.6(10)
O(16)−Eu(1)−N(10)	147.4(2)	O(18)−Eu(1)−N(10)	79.4(2)	N(10)−C(11′)−C(12′)	109.8(17)	N(1)−C(12)−C(11)	104.2(12)
O(20)−Eu(1)−N(10)	64.3(2)	N(1)−Eu(1)−N(10)	67.8(2)	N(1)−C(12′)−C(11′)	112.3(14)	N(1)−C(14)−N(14)	109.6(7)
N(4)−Eu(1)−N(10)	104.3(2)	N(7)−Eu(1)−N(10)	67.8(3)	Eu(1)−C(14)−O(14)	37.8(4)	Eu(1)−C(14)−N(14)	158.9(6)
O(1)−Eu(1)−C(14)	85.2(2)	O(14)−Eu(1)−C(14)	18.5(2)	O(14)−C(14)−N(14)	121.2(7)	Eu(1)−C(14)−C(13)	82.0(4)
O(16)−Eu(1)−C(14)	100.9(2)	O(18)−Eu(1)−C(14)	152.4(2)	O(14)−C(14)−C(13)	119.7(7)	N(14)−C(14)−C(13)	119.2(7)
O(2)−Eu(1)−C(14)	77.0(2)	N(1)−Eu(1)−C(14)	47.2(2)	N(4)−C(15)−C(16)	110.0(8)	Eu(1)−C(16)−O(16)	39.3(4)
N(4)−Eu(1)−C(14)	80.3(3)	N(7)−Eu(1)−C(14)	143.8(2)	Eu(1)−C(16)−N(16)	159.5(6)	O(16)−C(16)−N(16)	122.5(8)
N(10)−Eu(1)−C(14)	107.3(2)	O(1)−Eu(1)−C(16)	81.2(2)	Eu(1)−C(16)−C(15)	81.0(5)	O(16)−C(16)−C(15)	119.2(7)
O(14)−Eu(1)−C(16)	72.9(2)	O(16)−Eu(1)−C(16)	19.3(2)	N(16)−C(16)−C(15)	118.3(8)	N(7)−C(17)−C(18)	109.4(7)
O(18)−Eu(1)−C(16)	101.7(2)	O(20)−Eu(1)−C(16)	148.6(2)	Eu(1)−C(18)−O(18)	39.4(4)	Eu(1)−C(18)−N(18)	158.2(7)
N(1)−Eu(1)−C(16)	106.3(2)	N(4)−Eu(1)−C(16)	47.8(3)	O(18)−C(18)−N(18)	121.8(9)	Eu(1)−C(18)−C(17)	83.3(5)
N(7)−Eu(1)−C(16)	82.9(3)	N(10)−Eu(1)−C(16)	147.0(2)	O(18)−C(18)−C(17)	121.5(8)	N(18)−C(18)−C(17)	116.7(8)
C(14)−Eu(1)−C(16)	87.1(2)	O(1)−Eu(1)−C(18)	82.2(2)	N(10)−C(19)−C(20)	111.3(7)	Eu(1)−C(20)−O(20)	40.9(4)
O(14)−Eu(1)−C(18)	150.0(2)	O(16)−Eu(1)−C(18)	72.7(2)	Eu(1)−C(20)−N(20)	148.3(6)	O(20)−C(20)−N(20)	120.6(8)
O(18)−Eu(1)−C(18)	19.0(2)	O(20)−Eu(1)−C(18)	100.6(2)	Eu(1)−C(20)−C(19)	84.6(5)	O(20)−C(20)−C(19)	120.9(7)
N(1)−Eu(1)−C(18)	145.4(2)	N(4)−Eu(1)−C(18)	105.9(3)	N(20)−C(20)−C(19)	118.4(7)	O(1A)−S(1A)−O(2A)	113.9(5)
N(7)−Eu(1)−C(18)	47.3(3)	N(10)−Eu(1)−C(18)	82.3(2)	O(1A)−S(1A)−O(3A)	115.6(5)	O(2A)−S(1A)−O(3A)	114.7(4)
C(14)−Eu(1)−C(18)	167.3(2)	C(16)−Eu(1)−C(18)	89.0(2)	O(1A)−S(1A)−C(1A)	104.2(5)	O(2A)−S(1A)−C(1A)	102.2(4)
O(1)−Eu(1)−C(20)	81.4(2)	O(14)−Eu(1)−C(20)	104.8(2)	O(3A)−S(1A)−C(1A)	103.9(5)	S(1A)−C(1A)−F(2A)	110.7(7)
O(16)−Eu(1)−C(20)	145.1(2)	O(18)−Eu(1)−C(20)	69.1(2)	S(1A)−C(1A)−F(2A)	112.5(7)	F(1A)−C(1A)−F(2A)	108.6(9)
O(20)−Eu(1)−C(20)	20.3(2)	N(1)−Eu(1)−C(20)	87.7(2)	S(1A)−C(1A)−F(3A)	112.0(8)	F(1A)−C(1A)−F(3A)	105.3(9)
N(4)−Eu(1)−C(20)	149.9(3)	N(7)−Eu(1)−C(20)	105.0(3)	F(2A)−C(1A)−F(3A)	107.3(9)	O(1B)−S(1B)−O(2B)	114.6(5)
N(10)−Eu(1)−C(20)	48.5(2)	C(14)−Eu(1)−C(20)	94.9(2)	O(1B)−S(1B)−O(3B)	112.9(6)	O(2B)−S(1B)−O(3B)	116.3(6)
C(16)−Eu(1)−C(20)	162.3(2)	C(18)−Eu(1)−C(20)	85.2(2)	O(1B)−S(1B)−C(1B)	103.7(8)	O(2B)−S(1B)−C(1B)	105.0(6)
Eu(1)−O(14)−C(14)	123.7(5)	Eu(1)−O(16)−C(16)	121.4(5)	O(3B)−S(1B)−C(1B)	102.2(9)	S(1B)−C(1B)−F(1B)	109.7(13)
Eu(1)−O(18)−C(18)	121.6(5)	Eu(1)−O(20)−C(20)	118.8(5)	S(1B)−C(1B)−F(2B)	110.0(14)	F(1B)−C(1B)−F(2B)	106.1(15)
Eu(1)−N(1)−C(2)	107.4(7)	Eu(1)−N(1)−C(2′)	119.1(10)	S(1B)−C(1B)−F(3B)	113.0(12)	F(1B)−C(1B)−F(3B)	110.0(18)
Eu(1)−N(1)−C(12)	118.5(8)	C(2)−N(1)−C(12)	103.9(10)	F(2B)−C(1B)−F(3B)	107.8(16)	O(1C)−S(1C)−O(2C)	109.5(6)
Eu(1)−N(1)−C(12′)	102.5(8)	C(2′)−N(1)−C(12′)	110.6(13)	O(1C)−S(1C)−O(3C)	123.2(6)	O(2C)−S(1C)−O(3C)	110.2(6)
Eu(1)−N(1)−C(13)	106.4(5)	C(2)−N(1)−C(13)	101.2(8)	O(1C)−S(1C)−C(1C)	103.8(6)	O(2C)−S(1C)−C(1C)	104.3(6)
C(12)−N(1)−C(13)	117.6(9)	Eu(1)−N(4)−C(3)	119.6(8)	O(3C)−S(1C)−C(1C)	103.9(6)	S(1C)−C(1C)−F(1C)	112.2(11)
Eu(1)−N(4)−C(3′)	101.6(8)	Eu(1)−N(4)−C(5)	105.4(7)	S(1C)−C(1C)−F(2C)	111.4(10)	F(1C)−C(1C)−F(2C)	105.0(15)
C(3)−N(4)−C(5)	99.6(10)	Eu(1)−N(4)−C(5′)	125.0(11)	S(1C)−C(1C)−F(3C)	114.5(10)	F(1C)−C(1C)−F(3C)	106.8(12)
C(3′)−N(4)−C(5′)	105.2(13)	Eu(1)−N(4)−C(15)	105.6(6)	F(2C)−C(1C)−F(3C)	106.2(13)		
C(3)−N(4)−C(15)	120.2(9)	C(5)−N(4)−C(15)	103.8(9)				

the macrocyclic ring. These nitrogen atoms are essentially coplanar (rms deviation 0.015 Å). The four oxygen atoms of the pendent amide groups define the next four coordination sites; these are coplanar within 0.020 Å, and the plane of these four oxygen atoms is nearly parallel with that of the four nitrogen atoms (interplanar angle = 0.7°). The relative rotational orientation of the N_4 and O_4 moieties may be defined by the interplanar angles N(1)−Eu(1)−N(7)/O(14)−Eu(1)−O(18) = 30.4° and N(4)−Eu(1)−N(10)/O(16)−Eu(1)−O(20) = 30.2° (average angle, $\phi = 30.3°$.) Thus, the geometry is slightly closer to the capped square antiprismatic geometry ($\phi_{ideal} = 45°$) than to the capped square prismatic geometry ($\phi_{ideal} = 0°$).

The average Eu−N distance in the $[Eu(TCMC)(H_2O)]^{3+}$ cation is 2.651 ± 0.010 Å. The europium ion lies 1.639 Å from the N_4 plane. The average Eu−O(amide) distance is 2.392 ± 0.011 Å. The europium ion lies 0.793 Å from the O_4 plane. The apical Eu−O(H_2O) distance of 2.442(6) Å is comparable with those of similar complexes, including the cation $[Eu(THP)(H_2O)]^{3+}$ [19] (2.512(14) and 2.502(12) Å) and the anion $[Eu(DOTA)(H_2O)]^-$ [33] (2.480(3) Å). The average angles at europium from nitrogen atoms in the macrocyclic ring are N−Eu−N(cis) = 67.5 ± 0.3° and N−Eu−N(trans) = 103.6 ± 1.0°. The average O−Eu−O(trans) angle is 141.3 ± 1.6°. Finally, we note that the O(H_2O)−Eu−O(amide) angles are essentially equivalent, with O(1)−Eu(1)−O (14) = 71.7(2)°, O(1)−Eu(1)−O(16) = 69.3(2)°, O(1)−Eu(1)−O(18) = 70.7(2)° and O(1)−Eu(1)−O(20) = 70.8(2)°.

Luminescence Studies. The ground state $^7F_0$ and the excited state $^5D_0$ of the europium(III) ion are nondegenerate and are not split by ligand field effects. Each Eu(III) environment may, in theory, give rise to a different peak in an $^7F_0 \rightarrow {}^5D_0$ excitation spectrum,[34] and the number of excitation peaks may reflect the number of Eu(III) species present. The excitation band for a single crystal of $[Eu(TCMC)(H_2O)](CF_3SO_3)_3 \cdot 2CH_3OH$ (Figure 3) is resolved into two peaks. There are two different diastereomers of the $[Eu(TCMC)(H_2O)]^{3+}$ cation in the solid state structure, and each apparently gives rise to a separate excitation peak. In solution at pH 6.33, the excitation spectrum of the europium(III) TCMC complex has a band that is resolved into two peaks. (Figure 4). The excitation spectrum remains

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(33) Spirlet, M.-R.; Rebizant, J.; Desreux, J. F.; Loncin, M.-F. *Inorg. Chem.* **1984**, *23*, 359−363.

(34) Horrocks, W. DeW., Jr.; Sudnick, D. R. *Acc. Chem. Res.* **1981**, *14*, 384−392.

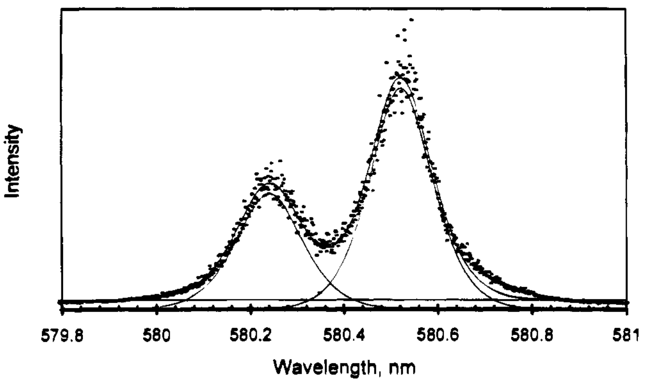

Figure 3. $^7F_0 \rightarrow {}^5D_0$ excitation spectrum (λ_{em} = 614 nm) of a single crystal of $[Eu(TCMC)(H_2O)](CF_3SO_3)_3 \cdot 2CH_3OH$ of approximate dimensions 0.2 mm × 0.2 mm × 0.15 mm at 37 °C. Peak maxima are at 580.24 and 580.52 nm.

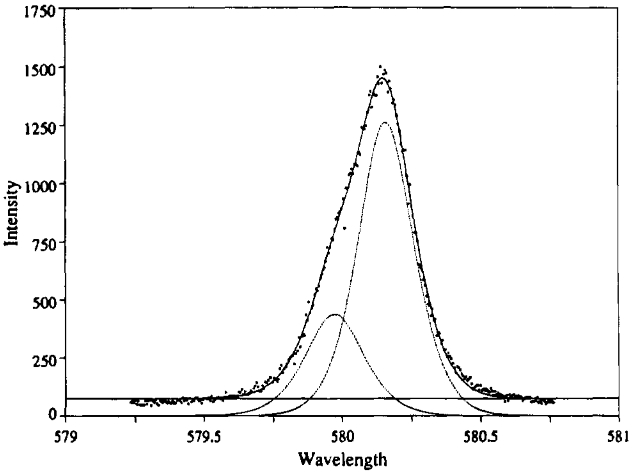

Figure 4. $^7F_0 \rightarrow {}^5D_0$ excitation spectrum (λ_{em} = 614 nm) of a solution of $[Eu(TCMC)]^{3+}$ (0.01 mM) at pH 6.33. Peak maxima are at 579.96 and 580.14 nm.

unchanged over the pH range 6.33–8.60, consistent with potentiometric titration experiments which suggest that there are no titratable protons and hence no metal hydroxide formation in this pH range.[22]

The method reported by Horrocks and Sudnick[35] for the determination of the number of OH oscillators coordinated to Eu(III) involves measurement of the luminescence lifetimes of the complexes in H_2O and in D_2O. In this method, the vibronic deexcitation pathway of the OH oscillators is eliminated by replacement of OH with OD. The number of coordinated water molecules (q in eq 3) or, alternately, the number of OH oscillators is estimated from these measurements.

$$q = 1.05(\tau^{-1}(H_2O) - \tau^{-1}(D_2O)) \qquad (3)$$

A single excited state lifetime is observed for $[Eu(TCMC)]^{3+}$ in solution. This would suggest that the two species in solution giving rise to the two excitation peaks are in rapid exchange on the luminescence time scale. At pH 6.33 τ^{-1} (H_2O) is 1.93 ms^{-1} and $\tau^{-1}(D_2O)$ is 0.46 ms^{-1}. Luminescence lifetimes at several pH values are given in the supplementary section.[36] The number of europium-bound water molecules is invariant at 1.5 ± 0.5 in the pH range 6.33–8.60.

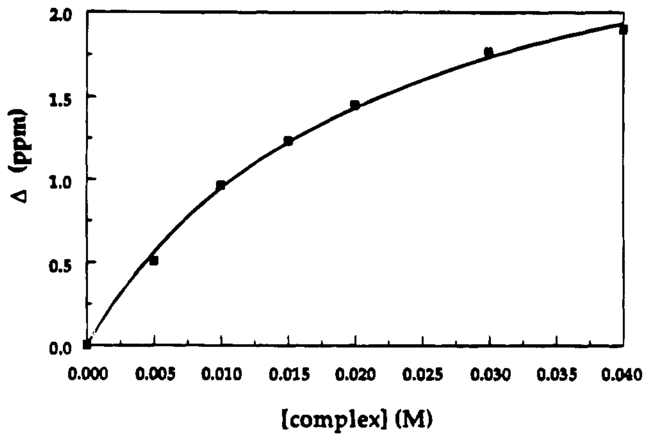

Figure 5. Plot of the change in ^{31}P NMR chemical shift ($\Delta = \delta_P - \delta_{obs}$) of diethyl phosphate (2.5 mM) at pH 7.4, 18 ± 2 °C, upon addition of $[La(L^1)]^{3+}$.

Binding Studies. Binding of diethyl phosphate to lanthanide(III) complexes including $[Eu(TCMC)]^{3+}$, $[La(TCMC)]^{3+}$, $[Eu(L^1)]^{3+}$, and $[La(L^1)]^{3+}$ was followed by use of ^{31}P NMR with trimethyl phosphate as an internal standard. The ^{31}P NMR peak of diethyl phosphate (10.0 mM) shifted upfield by 0.594 ppm upon addition of 20 mM $[La(TCMC)]^{3+}$ and by 2.522 ppm upon addition of 0.40 mM $[Eu(L^1)]^{3+}$. In contrast, the ^{31}P NMR resonance of diethyl phosphate (10 mM) did not shift upon addition of $[Eu(TCMC)]^{3+}$ (<0.01 ppm) in solutions containing 20 mM complex.

A binding constant was obtained for the coordination of $[La(L^1)]^{3+}$ to diethyl phosphate. Figure 5 shows the change in the ^{31}P NMR chemical shift of diethyl phosphate ($\delta_P - \delta_{obs}$) as a function of increasing lanthanum(III) complex concentrations. Fitting of the binding curve to eq 2 by a nonlinear curve-fitting program gave a binding constant of 47.7 ± 0.5 M^{-1} and Δ_{max} of 2.95 ± 0.05 ppm. For the $[La(TCMC)]^{3+}$ complex it was not possible to observe the full binding isotherm at reasonably low concentrations of complex (<40 mM). The extreme line broadening of the ^{31}P resonance of diethyl phosphate in the presence of $[Eu(L^1)]^{3+}$ prevented us from determining a binding constant for this europium(III) complex by use of ^{31}P NMR methods.

Discussion

The coordination geometry of the $[Eu(TCMC)(H_2O)]^{3+}$ cation is similar to that observed for the $[Eu(THP)(H_2O)]^{3+}$ cation (THP = 1,4,7,10-tetrakis(2-hydroxypropyl)-1,4,7,10-tetraazacyclododecane),[19] the $[Ln(DOTA)]^-$ anions (Ln = Eu, Y, Gd),[33,37] and the neutral Gd(III) complex of a DOTA derivative.[38] In these complexes the lanthanide(III) ions are nine-coordinate with coordination polyhedra that are best described as distorted square antiprisms capped by a water molecule. For the Eu(III) complexes of THP and TCMC, there are four stereoisomers of the europium(III) complex cations, including two enantiomeric pairs. The stereoisomers of the complex cations arise from the two different conformations of the tetraazamacrocycle ring in conjunction with the clockwise or counterclockwise orientation of the pendent amide or hydroxypropyl groups. The Gd(III) complex of (1*R*,4*R*,7*R*)-α,α′,α″-trimethyl-1,4,7,10-tetraazacyclododecane-1,4,7-triacetic acid[39] is an example of a similar lanthanide(III) complex that has two

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different conformations of the tetraazacyclododecane ring in the solid state. Interestingly, each of the two diastereomers of the $[Eu(TCMC)(H_2O)]^{3+}$ cation in a single crystal of $[Eu(TCMC)(H_2O)](CF_3SO_3)_3 \cdot 2CH_3OH$ gives rise to a separate laser-induced luminescence excitation peak. This is somewhat surprising given that the coordination environments of the Eu^{3+} ions are so similar.

Laser-induced luminescence lifetime studies suggest that one to two water molecules are bound to Eu(III) in aqueous solutions of $[Eu(TCMC)]^{3+}$, in reasonable agreement with the single bound water molecule in the solid state structure of the $[Eu(TCMC)(H_2O)]^{3+}$ cation. Solutions of $[Eu(TCMC)]^{3+}$ exhibit an excitation spectrum with a band that is resolved into two peaks; the peak at 580.14 nm corresponds closely to the peak at 580.24 nm in the excitation spectrum of the single crystal. Thus, it is possible that one of the $[Eu(TCMC)]^{3+}$ solution species is structurally similar to one of the cations in the solid state. The solution species that gives rise to the peak at 579.96 nm may have one more bound water molecule than the first solution species discussed above. Alternately, there may be more than one arrangement of the pendent groups of the macrocyclic complex. This has been suggested for the $[Ln(DOTA)]^-$ complexes[40] and for $[Tb(DOTMA)]^-$ (DOTMA = $[1R\text{-}(1R,4R,7R,10R)]\text{-}\alpha,\alpha',\alpha'',\alpha'''$-tetramethyl-1,4,7,10-tetraazacyclododecane-1,4,7,10-tetraacetate).[41]

Attempts have been made to correlate the frequency of the $^7F_0 \rightarrow {}^5D_0$ transition of Eu(III) complexes and the total ligand charge[42] by use of an empirical equation. Although this relationship bears out for many Eu(III) complexes, there appear to be several exceptions,[43] including a series of Eu(III) amide macrocyclic complexes.[44] The $[Eu(TCMC)(H_2O)]^{3+}$ complex is another exception for which this simple relationship between frequency and formal ligand charge does not hold. A new empirical equation correlating frequency and the sum of the derived nephelauxetic parameters of the ligating atoms was very recently reported.[43] This relationship promises to be successful for a wide range of Eu(III) complexes with different geometries and ligating groups. Use of this new relationship and parameters for ligating atoms leads to a prediction of 17 252 cm^{-1} for the frequency of the $^7F_0 \rightarrow {}^5D_0$ transition in the $[Eu(TCMC)(H_2O)]^{3+}$ complex. Comparison with the observed frequency of 17 240 cm^{-1} (an average of the two peaks in solution) suggests that the agreement is poor relative to those of most of the other Eu(III) complexes studied. Efforts are underway to study a larger series of Eu(III) amide complexes in order to derive more suitable parameters for amide ligating groups.

Diethyl phosphate was employed for binding studies as this simple phosphate diester is inert to hydrolysis in the presence of the lanthanide(III) complexes. $[La(L^1)]^{3+}$, $[Eu(L^1)]^{3+}$, and $[La(TCMC)]^{3+}$ bind to diethyl phosphate in water at 18 °C as demonstrated by use of ^{31}P NMR spectroscopy. That $[Eu(TCMC)]^{3+}$ does not bind to diethyl phosphate is consistent with the relatively low Lewis acidity of the complex as indicated by the high pK_a of its bound water molecule ($pK_a > 9.0$). In addition, the Eu(III) ion in $[Eu(TCMC)]^{3+}$ is nearly encapsulated by the macrocyclic ligand, with a single bound water molecule in the solid state and one to two bound water molecules in solution. The solid state structures of the complexes that bind diethyl phosphate, including $[La(TCMC)]^{3+}$, $[La(L^1)]^{3+}$, and $[Eu(L^1)]^{3+}$, have lanthanide ions that in the solid state contain at least two coordination sites in a cis orientation for binding substrates.[22,23,45] Laser-induced luminescence studies of $[Eu(L^1)]^{3+}$ in aqueous solution suggest that approximately three water molecules (2.8 ± 0.5) are bound to europium(III) at pH 7.4.[46]

Metal ion binding to a phosphate diester is generally the first step in transesterification or hydrolysis of the ester by metal ions.[21,47-50] Metal ion complexes that do not have coordination sites for the direct binding of the phosphate ester substrate are relatively inefficient at promoting phosphate diester transesterification. For example, the $[Co(NH_3)_5(OH)]^{2+}$ complex is kinetically inert to ligand exchange and does not promote phosphate diester transesterification at 37 °C, pH 6.85.[47] Thus, the inactivity of the $[Eu(TCMC)]^{3+}$ complex as a promoter for phosphate diester transesterification may be attributed to the fact that it does not coordinate directly to the phosphate diester. In contrast, the lanthanide(III) complexes that bind to diethyl phosphate, including $[La(TCMC)]^{3+}$, $[La(L^1)]^{3+}$, and $[Eu(L^1)]^{3+}$, have been shown to promote or catalyze rapid RNA cleavage.[15,22]

The constant for $[La(L^1)]^{3+}$ binding to diethyl phosphate (47.7 ± 0.5 M^{-1}) as determined by ^{31}P NMR methods falls in the range of phosphate diester binding constants of most di- and trivalent metal ions. Phosphate diester binding constants[48-50] for Mn(II), Cu(II), and Co(III) amine complexes are 11 (or 20), 20, and 4 M^{-1}, respectively. Phosphate diester binding constants for the trivalent lanthanide ions are typically higher than those of the metal ions listed above. For the phosphate diester 2-hydroxypropyl 4-nitrophenyl phosphate, binding constants of 73 M^{-1} for a La(III) salt and 62−130 M^{-1} for lanthanide(III) complexes have been reported.[21,47] In addition, binding constants for lanthanide ions to a dinucleotide of DNA were recently reported: 30 M^{-1}, Ce; 80 M^{-1}, Eu.[13] Work is underway to prepare a Eu(III) complex of a TCMC derivative with one fewer amide group. We would predict that the use of a heptadentate ligand will increase the number of coordination sites for binding small molecules and enhance the catalytic activity of Eu(III) macrocyclic complexes bearing amide pendent groups.

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Supplementary Material Available: Listings of anisotropic thermal parameters, calculated hydrogen atom positions, binding data, and luminescence lifetimes (4 pages). Ordering information is given on any current masthead page.

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